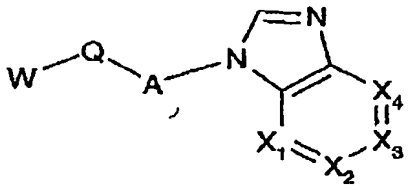
CLAIMS

1. A compound of the general formula I

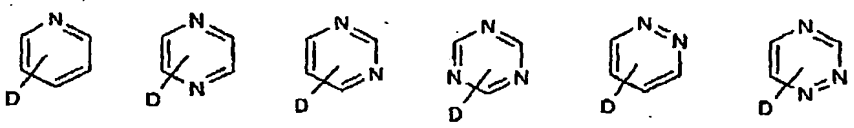


I

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

X_1, X_2, X_3, X_4 are each carbon where one is substituted with Z and the rest independently with Y; or one of X_1, X_2, X_3, X_4 is N, and the others are carbon where one carbon is substituted with Z and the rest independently with Y;

A is a ring selected from:



where D is selected from H, C_{1-4} alkyl, halogen, amino;

Q is a bond, halogen, C_{1-4} alkyl, O, S, SO, SO_2, CO, CS;

W is:

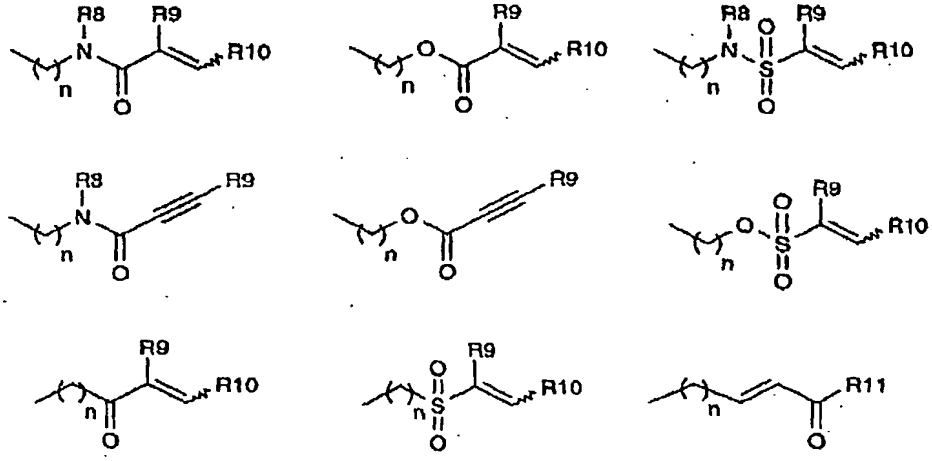
(ii) NR1R2 where R1 and R2 are independently H, C_{1-4} alkyl, C_{1-4} alkylCF_3, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl, C_{3-8} cycloalkyl, C_{2-6} alkenyl, cyclohetalkyl, C_{1-4} alkylcycloalkyl, C_{1-4} alkyl cyclohetalkyl, or R1 and R2 are joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR3; and R3 is selected from H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, COR4 where R4 is selected from H, C_{1-4} alkyl, aryl, hetaryl;

OR

(ii) H, C_{1-4} alkyl, aryl, hetaryl, C_{3-8} cycloalkyl, cyclohetalkyl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl, C_{3-8} cycloalkyl, C_{1-4} alkylcycloalkyl, C_{1-4} alkyl cyclohetalkyl;

Y is H, halogen, CN, CF_3, nitro, OH, C_{1-4} alkyl, C_{1-4} alkylNR5R6, C_{1-4} alkylhetaryl, OC_{1-4} alkyl, OC_{2-4} alkylOC_{1-4}alkyl, OC_{1-4} alkylNR5R6, OC_{1-4} alkylhetaryl, OC_{1-4} alkylcyclohetalkyl, SC_{1-4} alkyl, SC_{2-4} alkylOC_{1-4}alkyl, SC_{1-4} alkylNR5R6, NR5R6, NR5COR6, $NR5SO_2R6$; and R5 and R6 are each independently H, C_{1-4} alkyl, or may be joined to form an optionally substituted 3-6 membered ring optionally containing an atom selected from O, S, NR7 and R7 is selected from H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl;

Z is selected from :



where R8 is selected from H, C_{1-4} alkyl;

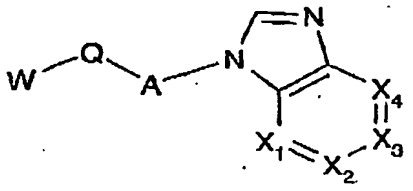
R9 and R10 are independently selected from H, C_{1-4} alkyl, C_{1-4} alkylNR12R13, C_{1-4} alkylOR12, C_{1-4} alkylhetaryl or may be joined to form a 5-8 membered ring optionally containing an atom selected from O, S, SO, SO_2, NR14;

R11 is selected from OH, OC_{1-4} alkyl, NR12R13;

n is 0-4;

where R12 and R13 are independently selected from H, C_{1-4} alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14; and R14 is selected from H, C_{1-4} alkyl.

2. A compound according to claim 1 wherein the compound of formula I is a compound of formula II:

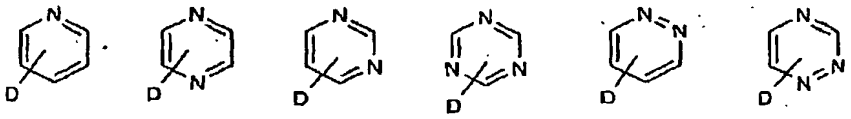


II

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

X_1, X_2, X_3, X_4 are each carbon where one is substituted with Z and the rest independently with Y; or one of X_1, X_2, X_3, X_4 is N, and the others are carbon where one carbon is substituted with Z and the rest independently with Y;

A is a ring selected from:



where D is selected from H, C_{1-4} alkyl, halogen, amino;

Q is a bond, halogen, C_{1-4} alkyl, O, S, SO, SO_2, CO, CS;

W is:

(ii) NR1R2 where R1 and R2 are independently H, C_{1-4} alkyl, C_{1-4} alkylCF_3, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl, C_{3-8} cycloalkyl, C_{2-6} alkenyl, cyclohetalkyl, C_{1-4} alkylcycloalkyl, C_{1-4} alkyl cyclohetalkyl, or R1 and R2 are joined to form an optionally substituted 3-8 membered ring optionally

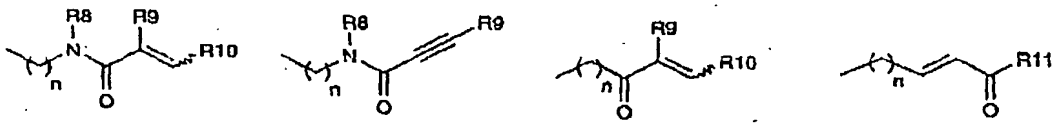
containing an atom selected from O, S, NR3; and R3 is selected from H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkyl aryl, C_{1-4} alkyl hetaryl, COR4 where R4 is selected from H, C_{1-4} alkyl, aryl, hetaryl;

OR

(ii) W is H, C_{1-4} alkyl, aryl, hetaryl, C_{3-8} cycloalkyl, cyclohetalkyl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl, C_{3-8} cycloalkyl, C_{1-4} alkylcycloalkyl, C_{1-4} alkyl cyclohetalkyl;

Y is H, halogen, CN, CF_3, nitro, OH, C_{1-4} alkyl, C_{1-4} alkylNR5R6, C_{1-4} alkylhetaryl, OC_{1-4} alkyl, OC_{2-4} alkylOC_{1-4}alkyl, OC_{1-4} alkylNR5R6, OC_{1-4} alkylhetaryl, OC_{1-4} alkylcyclohetalkyl, SC_{1-4} alkyl, SC_{2-4} alkylOC_{1-4}alkyl, SC_{1-4} alkylNR5R6, NR5R6, NR5COR6, $NR5SO_2R6$; and R5 and R6 are each independently H, C_{1-4} alkyl, or may be joined to form an optionally substituted 3-6 membered ring optionally containing an atom selected from O, S, NR7 and R7 is selected from H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl;

Z is selected from :



where R8 is selected from H, C_{1-4} alkyl;

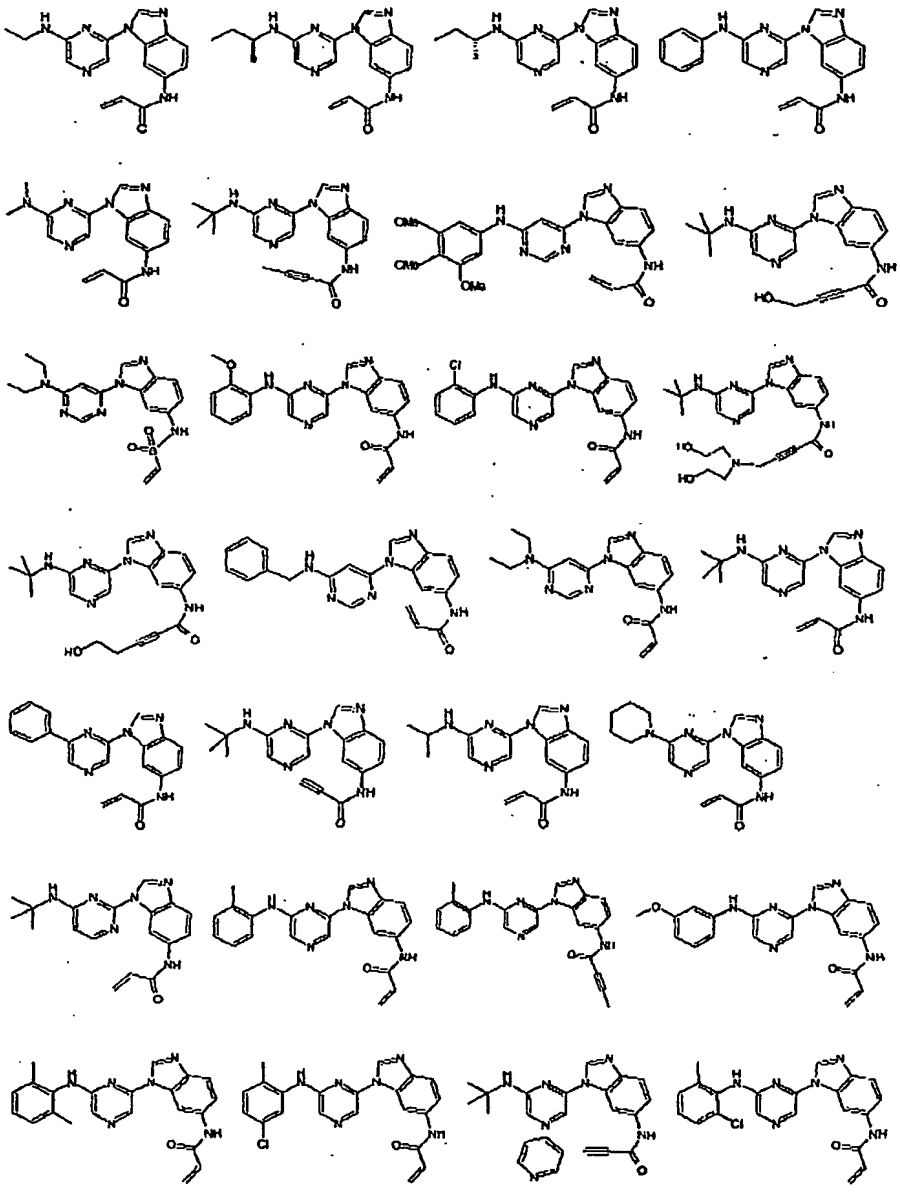
R9 and R10 are independently selected from H, C_{1-4} alkyl, C_{1-4} alkylNR12R13, C_{1-4} alkylOR12, C_{1-4} alkylhetaryl or may be joined to form a 5-8 membered ring optionally containing an atom selected from O, S, SO, SO_2, NR14;

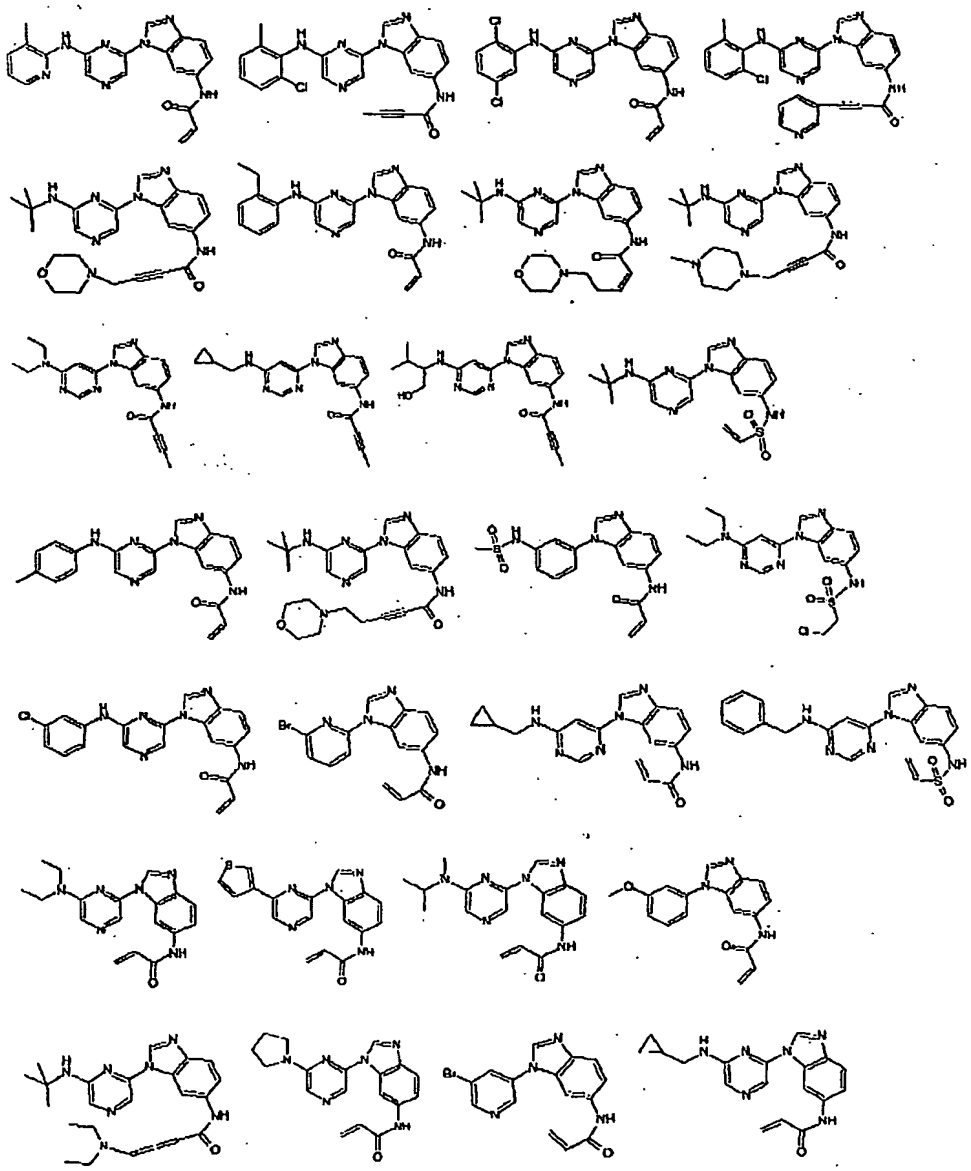
R11 is selected from OH, OC_{1-4} alkyl, NR12R13;

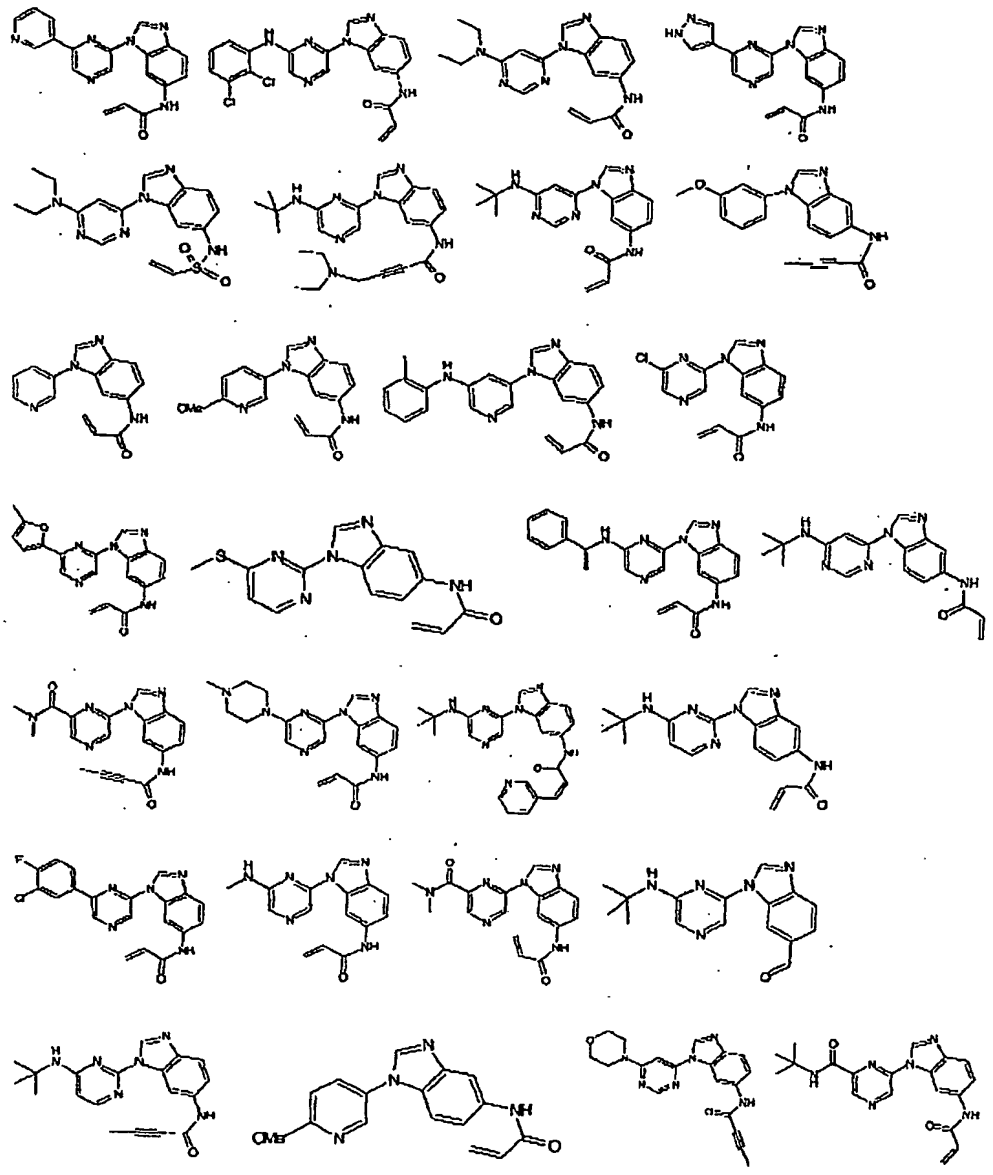
n is 0-4;

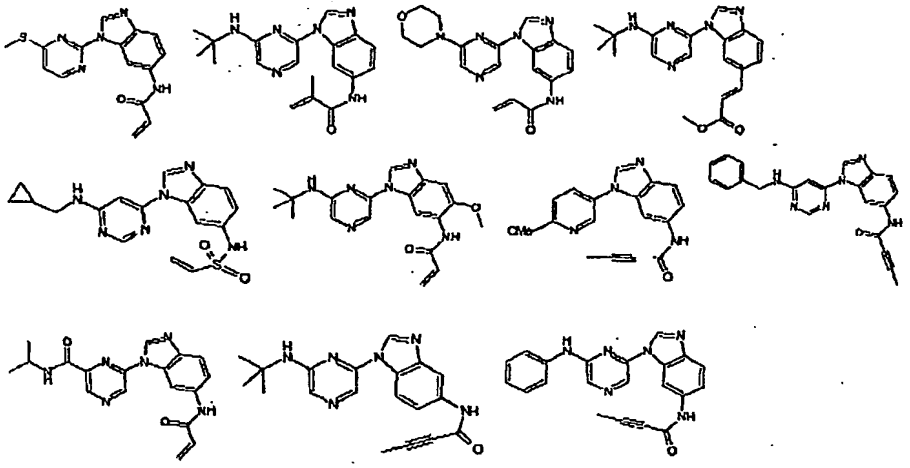
where: R12 and R13 are independently selected from H, C_{1-4} alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14; and R14 is selected from H, C_{1-4} alkyl.

3. A compound according to claim 1 selected from the group consisting of:









4. A compound according to any one of claims 1 to 3 wherein the compound irreversibly inhibits JAK-3.

5. A compound according to any one of claims 1 to 4 wherein the compound selectively inhibits JAK 3 with respect to JAK 1 or JAK 2.

6. A composition comprising a carrier and at least one compound according to any one of claims 1 to 5.

7. A method of treating a tyrosine kinase-associated disease state, the method comprising administering a therapeutically effective amount of at least one compound according to any one of claims 1 to 5 or a therapeutically effective amount of a composition according to claim 6.

8. Use of the compound according to any one of claims 1 to 5 or a composition according to claim 6 in the preparation of a medicament for the treatment of a JAK3-associated disease state.

9. A method of suppressing the immune system of a subject, the method comprising administering a therapeutically effective amount of at least one compound according to any one of claims 1 to 5 or a therapeutically effective amount of a composition according to claim 6.

AMENDED CLAIMS

[received by the International Bureau on 17 May 2005(17.05.05);
new claims 10-13 have been added; claims 1-9 remain unchanged (1 page)].

10. A selective JAK 3 inhibitor comprising a functionality wherein the functionality is positioned to selectively interact with the Cysteine residue close to the front lip of the ATP-binding cavity of JAK3 (CYS909) whereby the inhibitor is selective for JAK3 with respect to JAK2 and JAK1.

11. A selective JAK3 inhibitor according to claim 10 wherein the functionality irreversibly binds with the Cysteine residue.

12. A selective JAK3 inhibitor according to claim 10 or claim 11 wherein the functionality is an alkylating group.

13. A selective JAK3 inhibitor according to any one of claims 10 to 12 wherein the functionality is a Michael acceptor.